

Amendments

In the Claims:

Please substitute pending claims 3-13, 16-24, 29-31 and 33-37 with the following claims 3-13, 16-24, 29-31 and 33-37:

3. (Once amended) Method according to claim 1, characterized in that the prokaryotic cell is *E. coli*.

4. (Once amended) Method according to claim 1, characterized in that the following steps are carried out:

a) the DNA encoding the tPA, tPA variant, K2S molecule or K2S variant is amplified by PCR;

b) the PCR product is purified;

c) said PCR product is inserted into a vector comprising the DNA coding for OmpA signal peptide and the DNA coding for gpIII in such a way that said PCR product is operably linked upstream to the DNA coding for the OmpA signal sequence and linked downstream to the DNA coding for gpIII of said vector;

d) that a stop codon is inserted between said tPA, tPA variant, K2S molecule or K2S variant and gpIII;

e) said vector is expressed by the prokaryotic cell;

f) the tPA, tPA variant, K2S molecule or K2S variant is purified.

5. (Once amended) Method according to claim 1, characterized in that the vector is a phagemid vector comprising the DNA coding for OmpA signal peptide and the DNA coding for gpIII.

6. (Once amended) Method according to claim 1, characterised in that the vector is the pComb3HSS phagemid.

7. (Once amended) Method according to claim 1, characterized in that the DNA Sequence of OmpA linked upstream to K2S comprises the following sequence or a functional variant thereof or a variant due to the degenerate nucleotide code:

ATGAAAAAGACAGCTATCGCGATTGCAGTGGCACTGGCTGGTTTCGCTACCG
TGGCCCAGGCGGCCTCTGAGGGAAACAGTGACTGCTACTTTGGGAATGGGTC
AGCCTACCGTGGCACGCACAGCCTCACCGAGTCGGGTGCCTCCTGCCTCCCG
TGGAATTCCATGATCCTGATAGGCAAGGTTTACACAGCACAGAACCCCAGTG
CCCAGGCACTGGGCCTGGGCAAACATAATTACTGCCGGAATCCTGATGGGGA
TGCCAAGCCCTGGTGCCACGTGCTGAAGAACCGCAGGCTGACGTGGGAGTA
CTGTGATGTGCCCTCCTGCTCCACCTGCGGCCTGAGACAGTACAGCCAGCCT
CAGTTTCGCATCAAAGGAGGGGCTCTTCGCCGACATCGCCTCCCACCCCTGGC
AGGCTGCCATCTTTGCCAAGCACAGGAGGTGCGCCGGAGAGCGGTTCTCTGTG
CGGGGGCATACTCATCAGCTCCTGCTGGATTCTCTCTGCCGCCCCTGCTTCC
AGGAGAGGTTTCCGCCCCACCACCTGACGGTGATCTTGGGCAGAACATACCG
GGTGGTCCCTGGCGAGGAGGAGCAGAAATTTGAAGTCGAAAAATACATTGT
CCATAAGGAATTCGATGATGACACTTACGACAATGACATTGCGCTGCTGCAG
CTGAAATCGGATTCGTCCCGCTGTGCCCAGGAGAGCAGCGTGGTCCGCACTG
TGTGCCTTCCCCCGGCGGACCTGCAGCTGCCGGAAGTGGACGGAGTGTGAGCT
CTCCGGCTACGGCAAGCATGAGGCCTTGTCTCCTTTCTATTCTGGAGCGGCTG
AAGGAGGCTCATGTCAGACTGTACCCATCCAGCCGCTGCACATCACAACATT
TACTTAACAGAACAGTCACCGACAACATGCTGTGTGCTGGAGACACTCGGAG
CGGCGGGCCCCAGGCAAACCTTGACGACGCCTGCCAGGGGCGATTCGGGAGG
CCCCCTGGTGTGTCTGAACGATGGCCGCATGACTTTGGTGGGCATCATCAGC
TGGGGCCTGGGCTGTGGACAGAAGGATGTCCCGGGTGTGTACACAAAGGTTA
CCAACTACCTAGACTGGATTCGTGACAACATGCGACCG (SEQ ID NO:2)

8. (Once amended) Method according to claim 1, characterized in that the DNA Sequence of OmpA comprises the following sequence:

ATGAAAAAGACAGCTATCGCGATTGCAGTGGCACTGGCTGGTTTCGCTACCG
TGGCCCAGGCGGCC (SEQ ID NO:3)

9. (Once amended) Method according to claim 1, characterized in that the DNA Sequence of OmpA consists of the following sequence:

ATGAAAAAGACAGCTATCGCGATTGCAGTGGCACTGGCTGGTTTCGCTACCG
TGGCCCAGGCGGCC (SEQ ID NO:3)

10. (Once amended) Method according to claim 1, characterized in that the DNA of the tPA, tPA variant, K2S molecule or K2S variant is preceded by a lac promoter and/or a ribosomal binding site.

11. (Once amended) Method according to claim 1, characterised in that the DNA coding for the tPA, tPA variant, K2S molecule or K2S variant is selected from the group of DNA molecules coding for at least 90% of the amino acids 87 - 527, 174 - 527, 180 - 527 or 220 - 527 of the human tissue plasminogen activator protein.

12. (Once amended) Method according to claim 5, characterized in that the DNA Sequence of K2S comprises the following sequence or a functional variant thereof or a variant due to the degenerate nucleotide code:

TCTGAGGGAAACAGTGACTGCTACTTTGGGAATGGGTCAGCCTACCGTGG
CACGCACAGCCTCACCGAGTCGGGTGCCTCCTGCCTCCCGTGGAATTCCA
TGATCCTGATAGGCAAGGTTTACACAGCACAGAACCCAGTGCCCAGGC
ACTGGGCCTGGGCAAACATAATTACTGCCGGAATCCTGATGGGGATGCC
AAGCCCTGGTGCCACGTGCTGAAGAACCGCAGGCTGACGTGGGAGTACT
GTGATGTGCCCTCCTGCTCCACCTGCGGCCTGAGACAGTACAGCCAGCCT
CAGTTTCGCATCAAAGGAGGGCTCTTCGCCGACATCGCCTCCCACCCCTG
GCAGGCTGCCATCTTTGCCAAGCACAGGAGGTCGCCCCGAGAGCGGTTC
CTGTGCGGGGGCATACTCATCAGCTCCTGCTGGATTCTCTCTGCCGCCCA
CTGCTTCCAGGAGAGGTTTCCGCCCCACCACCTGACGGTGATCTTGGGCA
GAACATAACCGGGTGGTCCCTGGCGAGGAGGAGCAGAAATTTGAAGTCGA
AAAATACATTGTCCATAAGGAATTCGATGATGACACTTACGACAATGACA
TTGCGCTGCTGCAGCTGAAATCGGATTCGTCCCGCTGTGCCCAGGAGAGC

AGCGTGGTCCGCACTGTGTGCCTTCCCCCGGCGGACCTGCAGCTGCCGGA
CTGGACGGAGTGTGAGCTCTCCGGCTACGGCAAGCATGAGGCCTTGTCTC
CTTTCTATTCGGAGCGGCTGAAGGAGGCTCATGTCAGACTGTACCCATCC
AGCCGCTGCACATCACAACATTTACTTAACAGAACAGTCACCGACAACA
TGCTGTGTGCTGGAGACACTCGGAGCGGCGGGCCCCAGGCCAAACTTGCA
CGACGCCTGCCAGGGCGATTTCGGGAGGCCCCCTGGTGTGTCTGAACGAT
GGCCGCATGACTTTGGTGGGCATCATCAGCTGGGGCCTGGGCTGTGGAC
AGAAGGATGTCCCGGGTGTGTACACAAAGGTTACCAACTACCTAGACTG
GATTCGTGACAACATGCGACCGTGA (SEQ ID NO:4).

61 13. (Once amended) Method according to claim 5, characterized in that the DNA
Sequence of K2S consists of the following sequence:

TCTGAGGGAAACAGTGACTGCTACTTTGGGAATGGGTCAGCCTACCGTGG
CACGCACAGCCTCACCGAGTCGGGTGCCTCCTGCCTCCCGTGGAATTCCA
TGATCCTGATAGGCAAGGTTTACACAGCACAGAACCCAGTGCCAGGC
ACTGGGCCTGGGCAAACATAATTACTGCCGGAATCCTGATGGGGATGCC
AAGCCCTGGTGCCACGTGCTGAAGAACCGCAGGCTGACGTGGGAGTACT
GTGATGTGCCCTCCTGCTCCACCTGCGGCCTGAGACAGTACAGCCAGCCT
CAGTTTCGCATCAAAGGAGGGCTCTTCGCCGACATCGCCTCCCACCCCTG
GCAGGCTGCCATCTTTGCCAAGCACAGGAGGTCGCCCCGAGAGCGGTTC
CTGTGCGGGGGCATACTCATCAGCTCCTGCTGGATTCTCTCTGCCGCCCA
CTGCTTCCAGGAGAGGTTTCCGCCCCACCACCTGACGGTGATCTTGGGCA
GAACATAACCGGGTGGTCCCTGGCGAGGAGGAGCAGAAATTTGAAGTCGA
AAAATACATTGTCCATAAGGAATTCGATGATGACACTTACGACAATGACA
TTGCGCTGCTGCAGCTGAAATCGGATTCGTCCCGCTGTGCCAGGAGAGC
AGCGTGGTCCGCACTGTGTGCCTTCCCCCGGCGGACCTGCAGCTGCCGGA
CTGGACGGAGTGTGAGCTCTCCGGCTACGGCAAGCATGAGGCCTTGTCTC
CTTTCTATTCGGAGCGGCTGAAGGAGGCTCATGTCAGACTGTACCCATCC
AGCCGCTGCACATCACAACATTTACTTAACAGAACAGTCACCGACAACA
TGCTGTGTGCTGGAGACACTCGGAGCGGCGGGCCCCAGGCCAAACTTGCA

Q1
CGACGCCTGCCAGGGCGATTCTGGGAGGCCCCCTGGTGTGTCTGAACGAT
GGCCGCATGACTTTGGTGGGCATCATCAGCTGGGGCCTGGGCTGTGGAC
AGAAGGATGTCCCGGGTGTGTACACAAAGGTTACCAACTACCTAGACTG
GATTCGTGACAACATGCGACCGTGA (SEQ ID NO:4).

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16. (Once amended) DNA molecule according to claim 14, characterized in that said DNA sequence consists of the following sequence:

ATGAAAAAGACAGCTATCGCGATTGCAGTGGCACTGGCTGGTTTCGCTACCG
TGGCCCAGGCGGCCTCTGAGGGAAACAGTGACTGCTACTTTGGGAATGGGTC
AGCCTACCGTGGCACGCACAGCCTCACCGAGTCGGGTGCCTCCTGCCTCCCG
TGGAATTCCATGATCCTGATAGGCAAGGTTTACACAGCACAGAACCCCACTG
CCCAGGCACTGGGCCTGGGCAAACATAATTACTGCCGGAATCCTGATGGGGA
TGCCAAGCCCTGGTGCCACGTGCTGAAGAACCGCAGGCTGACGTGGGAGTA
CTGTGATGTGCCCTCCTGCTCCACCTGCGGCCTGAGACAGTACAGCCAGCCT
CAGTTTCGCATCAAAGGAGGGCTCTTCGCCGACATCGCCTCCCACCCCTGGC
AGGCTGCCATCTTTGCCAAGCACAGGAGGTCGCCCCGAGAGCGGTTCTGT
GCGGGGGCATACTCATCAGCTCCTGCTGGATTCTCTCTGCCGCCCCTGCTT
CCAGGAGAGGTTTCCGCCCCACCACCTGACGGTGATCTTGGGCAGAACATA
CCGGGTGGTCCCTGGCGAGGAGGAGCAGAAATTTGAAGTCGAAAAATACA
TTGTCCATAAGGAATTCGATGATGACACTTACGACAATGACATTGCGCTGC
TGCAGCTGAAATCGGATTTCGTCCTCGCTGTGCCAGGAGAGCAGCGTGGTCC
GCACTGTGTGCCTTCCCCCGGCGGACCTGCAGCTGCCGGAAGTGGACGGAGT
GTGAGCTCTCCGGCTACGGCAAGCATGAGGCCTTGTCTCCTTTCTATTCGGA
GCGGCTGAAGGAGGCTCATGTGCACTGTACCCATCCAGCCGCTGCACATC
ACAACATTTACTTAAACAGAACAGTCACCGACAACATGCTGTGTGCTGGAGAC
ACTCGGAGCGGCGGGCCCCAGGCAAACCTTGACGACGCCTGCCAGGGCGAT
TCGGGAGGCCCCCTGGTGTGTCTGAACGATGGCCGCATGACTTTGGTGGGCA
TCATCAGCTGGGGCCTGGGCTGTGGACAGAAGGATGTCCCGGGTGTGTACAC
AAAGGTTACCAACTACCTAGACTGGATTCGTGACAACATGCGACCG (SEQ ID
NO:5).

17. (Once amended) DNA molecule according to claim 14, characterized in that said DNA sequence b) is coding for at least 90% of the amino acids 87 - 527 of the human tissue plasminogen activator protein.

18. (Once amended) DNA molecule according to claim 14, characterized in that said DNA sequence b) is coding for at least 90% of the amino acids 174 - 527 of the human tissue plasminogen activator protein.

19. (Once amended) DNA molecule according to any claim 14, characterized in that said DNA sequence b) is coding for at least 90% of the amino acids 180 - 527 of the human tissue plasminogen activator protein.

20. (Once amended) DNA molecule according to claim 14, characterized in that said DNA sequence b) is coding for at least 90% of the amino acids 220 - 527 of the human tissue plasminogen activator protein.

21. (Once amended) DNA molecule according to claim 14, characterized in that said DNA sequence a) is hybridizing under stringent conditions to the following sequence:
ATGAAAAAGACAGCTATCGCGATTGCAGTGGCACTGGCTGGTTTCGCTACCG
TGGCCCAGGCGGCC (SEQ ID NO:6).

22. (Once amended) DNA molecule according to claim 14, characterized in that said DNA sequence a) consists of the following sequence:
ATGAAAAAGACAGCTATCGCGATTGCAGTGGCACTGGCTGGTTTCGCTACCG
TGGCCCAGGCGGCC (SEQ ID NO:6).

23. (Once amended) DNA molecule according to claim 14, characterized in that said DNA sequence b) is hybridizing under stringent conditions to the following sequence:
TCTGAGGGAAACAGTGACTGCTACTTTGGGAATGGGTCAGCCTACCGTGGC
ACGCACAGCCTACCGAGTCGGGTGCCTCCTGCCTCCCGTGAATTCCATG

ATCCTGATAGGCAAGGTTTACACAGCACAGAACCCCAGTGCCCAGGCACT
GGGCCTGGGCAAACATAATTACTGCCGGAATCCTGATGGGGATGCCAAGC
CCTGGTGCCACGTGCTGAAGAACCGCAGGCTGACGTGGGAGTACTGTGAT
GTGCCCTCCTGCTCCACCTGCGGCCTGAGACAGTACAGCCAGCCTCAGTTT
CGCATCAAAGGAGGGCTCTTCGCCGACATCGCCTCCCACCCCTGGCAGGCT
GCCATCTTTGCCAAGCACAGGAGGTCGCCCCGGAGAGCGGTTCTGTGCGGG
GGCATACTCATCAGCTCCTGCTGGATTCTCTCTGCCGCCCACTGCTTCCAGG
AGAGGTTTCCGCCCCACCACCTGACGGTGATCTTGGGCAGAACATAACGGG
TGGTCCCTGGCGAGGAGGAGCAGAAATTTGAAGTCGAAAAATACATTGTCC
ATAAGGAATTCGATGATGACACTTACGACAATGACATTGCGCTGCTGCAGCT
GAAATCGGATTCGTCCCGCTGTGCCCAGGAGAGCAGCGTGGTCCGCACTGTG
TGCTTCCCCCGGCGGACCTGCAGCTGCCGGACTGGACGGAGTGTGAGCTCT
CCGGCTACGGCAAGCATGAGGCCTTGTCTCCTTTCTATTTCGGAGCGGCTGAA
GGAGGCTCATGTCAGACTGTACCCATCCAGCCGCTGCACATCACAACATTTA
CTTAACAGAACAGTCACCGACAACATGCTGTGTGCTGGAGACACTCGGAGCG
GCGGGCCCCAGGCAAACCTTGACGACGCCTGCCAGGGCGATTCGGGAGGCC
CCCTGGTGTGTCTGAACGATGGCCGCATGACTTTGGTGGGCATCATCAGCTG
GGGCCTGGGCTGTGGACAGAAGGATGTCCCGGGTGTGTACACAAAGGTTAC
CAACTACCTAGACTGGATTCGTGACAACATGCGACCGTGA (SEQ ID NO:7).

24. (Once amended) DNA molecule according to claim 14, characterized in that said DNA sequence b) consists of the following sequence:

TCTGAGGGAAACAGTGACTGCTACTTTGGGAATGGGTCAGCCTACCGTGGC
ACGCACAGCCTCACCGAGTCGGGTGCCTCCTGCCTCCCGTGGAATTCCATG
ATCCTGATAGGCAAGGTTTACACAGCACAGAACCCCAGTGCCCAGGCACT
GGGCCTGGGCAAACATAATTACTGCCGGAATCCTGATGGGGATGCCAAGC
CCTGGTGCCACGTGCTGAAGAACCGCAGGCTGACGTGGGAGTACTGTGAT
GTGCCCTCCTGCTCCACCTGCGGCCTGAGACAGTACAGCCAGCCTCAGTTT
CGCATCAAAGGAGGGCTCTTCGCCGACATCGCCTCCCACCCCTGGCAGGCT
GCCATCTTTGCCAAGCACAGGAGGTCGCCCCGGAGAGCGGTTCTGTGCGGG

G2

GGCATACTCATCAGCTCCTGCTGGATTCTCTCTGCCGCCCCACTGCTTCCAGG
AGAGGTTTCCGCCCCACCACTGACGGTGATCTTGGGCAGAACATACCGGG
TGGTCCCTGGCGAGGAGGAGCAGAAATTTGAAGTCGAAAAATACATTGTCC
ATAAGGAATTCGATGATGACACTTACGACAATGACATTGCGCTGCTGCAGC
TGAAATCGGATTCGTCCCGCTGTGCCAGGAGAGCAGCGTGGTCCGCACTGT
GTGCCTTCCCCCGGCGGACCTGCAGCTGCCGGACTGGACGGAGTGTGAGCTC
TCCGGCTACGGCAAGCATGAGGCCTTGTCTCCTTTCTATTCCGGAGCGGCTGA
AGGAGGCTCATGTCAGACTGTACCCATCCAGCCGCTGCACATCACAACATTT
ACTTAACAGAACAGTCACCGACAACATGCTGTGTGCTGGAGACACTCGGAGC
GGCGGGCCCCAGGCAAACCTGCACGACGCCTGCCAGGGCGATTCGGGAGGC
CCCCTGGTGTGTCTGAACGATGGCCGCATGACTTTGGTGGGCATCATCAGCT
GGGGCCTGGGCTGTGGACAGAAGGATGTCCCGGGTGTGTACACAAAGGTTA
CCAACCTACCTAGACTGGATTCGTGACAACATGCGACCGTGA (SEQ ID NO:7).

Concluded

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29. (Once amended) K2S protein according to claim 27, characterized in that it comprises a protein characterized by the following amino acid sequence or a fragment, a functional variant, an allelic variant, a subunit, a chemical derivative or a glycosylation variant thereof:

SEGNSDCYFGNGSAYRGTHSLTESGASCLPWNSMILIGKVYTAQNPSAQUALGLG
KHNYCRNPDGDAKPWCHVLKNRRLTWEYCDVPSCSTCGLRQYSQPQFRIKGGL
FADIASHPWQAAIFAKHRRSPGERFLCGGILISSCWILSAAHCFQERFPPHHLTVIL
GRTYRVVPGEESQKFEVEKYIVHKEFDDDTYDNDIALQLKSDSSRCAQESSVV
RTVCLPPADLQLPDWTECELSGYGKHEALSPFYSERLKEAHVRLYPSSRCTSQHL
LNRTVTDNMLCAGDTRSGGPQANLHDACQGDSSGPLVCLNDGRMTLVGIISWG
LGCGQKDVPGVYTKVTNYLDWIRDNMRP* (SEQ ID NO:11).

30. (Once amended) K2S according to claim 27, characterized in that it consists of a protein characterized by the following amino acid sequence:

SEGNSDCYFGNGSAYRGTHSLTESGASCLPWNSMILIGKVYTAQNPSAQUALGLG
KHNYCRNPDGDAKPWCHVLKNRRLTWEYCDVPSCSTCGLRQYSQPQFRIKGGL

a3
FADIASHPWQAAIFAKHRRSPGERFLCGGILISSCWILSAAHCFQERFPPHHLTIVIL
GRTYRVVPGEQQKFEVEKYIVHKEFDDDTYDNDIALQLKSDSSRCAQESSVV
RTVCLPPADLQLPDWTECELSGYGKHEALSPFYSERLKEAHVRLYPSSRCTSQHL
LNRTVTDNMLCAGDTRSGGPQANLHDACQGDSGGPLVCLNDGRMTLVGIISWG
LGCGQKDVPGVYTKVTNYLDWIRDNMMP* (SEQ ID NO:11).

31. (Once amended) A vector containing a DNA sequence according to claim 14.

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33. (Once amended) The vector pComb3HSS containing a DNA according to claim 14, wherein the expression of the gp III protein is suppressed or inhibited by deleting the DNA molecule encoding said gp III protein or by a stop codon between the gene coding for a polypeptide containing the kringle 2 domain and the serine protease domain of tissue plasminogen activator protein and the protein III gene.

34. (Once amended) A prokaryotic host cell comprising a DNA molecule according to claim 14.

35. (Once amended) A prokaryotic host cell comprising a vector according to claim 31:

36. (Once amended) An *E. coli* host cell comprising a DNA molecule according to claim 14.

37. (Once amended) An *E. coli* host cell comprising a vector according to claim 31.

Please cancel claims 38 and 39.